Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1654	gray-j$.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:40
L2	747	mulligan-$.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:40
L3	45565	lee-j$.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:40
L4	40807	lee-s$.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:40
L5	86667	1 or 2 or (3 or 4)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:40
L6	2	1 and 2 and (3 or 4)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:42
L7	3939	codon with optimiz$4	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:41
L8	52	7 with (gagpol or gag or pol)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:42
L9	1	5 and 8	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:42
L10	37	5 and 7	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:42
L11	3	1 and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:43
L12	2791	("Children's" with Medical with Center).as. or (Harvard).as.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:44

L13	16	12 and 5	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:44
L14	0	7 and 13	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:44
L15	14	13 not (6 or 11)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:44
L16	44	(hiv or lentivir$4 or maloney or vecisular) with (codon-optimiz$6 or (codon adj2 optimiz$6))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:45
L17	65	(hiv or lentivir$4 or maloney or vecisular) same (codon-optimiz$6 or (codon adj2 optimiz$6))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:45
L18	624	(hiv or lentivir$4 or maloney or vecisular) and (codon-optimiz$6 or (codon adj2 optimiz$6))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:45
L19	30	((hiv or lentivir$4 or maloney or vecisular) same (codon-optimiz$6 or (codon adj2 optimiz$6))) not ((gag or pol) with (codon-optimiz$6 or (codon adj2 optimiz$6)))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:45
L20	85	biomedica-$.as.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:46
L21	53	mitrophanous-$.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:46
L22	4	kotsopoulou-$.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:46
L23	114	kingsman-a$.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:47
L24	165	kingsman-$.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:47

L25	125	kingsman-s$.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:47
L26	74	23 and 25	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:48
L27	153	(Oxford with biomedica).as.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:48
L28	238	20 or 27	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:48
L29	2961	kim-n$.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:48
L30	3121	21 or 22 or 23 or 24 or 25 or 29	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:49
L31	2	21 and 22 and 24 and 29	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:51
L32	6	30 and 8	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:55
L33	1290	"RRE" or (rev adj3 response adj3 element$1) or "RREs"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:58
L34	8156	"CTEs" or "CTE" or (constitutive with transport with element$1)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:56
L35	9370	33 or 34	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:56
L36	504	35 with (devoid or lack$4 or deficient or without)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:57

L37	14	30 and 36	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:58
L38	1	5 and 36	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 13:58
L39	14	37 and (lentivir$4 or retrovir$4 or HIV or (human adj2 immunodeficiency adj2 vir$4))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 14:06
L40	6	39 and 7	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 14:01
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L42	8	39 not 40	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 14:04
L43	3	"6669936".pn. or "6312682".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 14:04
L44	104	36 and (lentivir$4 or retrovir$4 or HIV or (human adj2 immunodeficiency adj2 vir$4))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 14:06
L45	7	36 and (lentivir$4 or retrovir$4 or HIV or (human adj2 immunodeficiency adj2 vir$4)) and 18	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/21 14:07

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 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  FEB 25   CA/CAPLUS - Russian Agency for Patents and Trademarks
                   (ROSPATENT) added to list of core patent offices covered
 NEWS  4  FEB 28   PATDPAFULL - New display fields provide for legal status
                   data from INPADOC
 NEWS  5  FEB 28   BABS - Current-awareness alerts (SDIs) available
 NEWS  6  FEB 28   MEDLINE/LMEDLINE reloaded
 NEWS  7  MAR 02   GBFULL: New full-text patent database on STN
 NEWS  8  MAR 03   REGISTRY/ZREGISTRY - Sequence annotations enhanced
 NEWS  9  MAR 03   MEDLINE file segment of TOXCENTER reloaded
 NEWS  10 MAR 22   KOREAPAT now updated monthly; patent information enhanced
 NEWS  11 MAR 22   Original IDE display format returns to REGISTRY/ZREGISTRY
 NEWS  12 MAR 22   PATDPASPC - New patent database available
 NEWS  13 MAR 22   REGISTRY/ZREGISTRY enhanced with experimental property tags
 NEWS  14 APR 04   EPFULL enhanced with additional patent information and new
                   fields
 NEWS  15 APR 04   EMBASE - Database reloaded and enhanced
 NEWS  16 APR 18   New CAS Information Use Policies available online

 NEWS EXPRESS  JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

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=> FILE MEDLINE EMBASE BIOSIS CAPLUS
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21
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'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
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L2         6393 (MULLIGAN, ?)/IN,AU

=> S (LEE, ?)/IN,AU
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L3       558398 (LEE, ?)/IN,AU

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L4       627388 L1 OR L2 OR L3

=> S L1 AND L2 AND L3
L5            5 L1 AND L2 AND L3

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KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):N
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=> D IBIB AB L6 1,2

L6   ANSWER 1 OF 2     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:    2004474995     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 15386015
TITLE:               Exogenous control of mammalian gene expression through
                     modulation of RNA self-cleavage.
COMMENT:             Comment in: Nature. 2004 Sep 23;431(7007):409. PubMed ID:
                     15385996
AUTHOR:              Yen Laising; Svendsen Jennifer; Lee Jeng-Shin;
                     Gray John T; Magnier Maxime; Baba Takashi; D'Amato
                     Robert J; Mulligan Richard C
CORPORATE SOURCE:    Department of Genetics, Harvard Institute of Human
                     Genetics, Harvard Medical School, and Division of Molecular
                     Medicine, Children's Hospital, Boston, Massachusetts 02115,
                     USA.
SOURCE:              Nature, (2004 Sep 23) 431 (7007) 471-6.
                     Journal code: 0410462. ISSN: 1476-4687.
PUB. COUNTRY:        England: United Kingdom
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
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ENTRY MONTH: 200410
ENTRY DATE: Entered STN: 20040924
Last Updated on STN: 20041006
Entered Medline: 20041005

AB Recent studies on the control of specific metabolic pathways in bacteria have documented the existence of entirely RNA-based mechanisms for controlling gene expression. These mechanisms involve the modulation of translation, transcription termination or RNA self-cleavage through the direct interaction of specific intracellular metabolites and RNA sequences. Here we show that an analogous RNA-based gene regulation system can effectively be designed for mammalian cells via the incorporation of sequences encoding self-cleaving RNA motifs into the transcriptional unit of a gene or vector. When correctly positioned, the sequences lead to potent inhibition of gene or vector expression, owing to the spontaneous cleavage of the RNA transcript. Administration of either oligonucleotides complementary to regions of the self-cleaving motif or a specific small molecule results in the efficient induction of gene expression, owing to inhibition of self-cleavage of the messenger RNA. Efficient regulation of transgene expression is shown in a variety of mammalian cell lines and live animals. In conjunction with other emerging technologies, this methodology may be particularly applicable to the development of gene regulation systems tailored to any small inducer molecule, and provide a novel means of biological sensing in vivo that may have an important application in the regulated delivery of protein therapeutics.

L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:575260 CAPLUS
DOCUMENT NUMBER: 137:136065
TITLE: Retroviral vectors containing SNV gag-pol capable of transducing therapeutic genes into quiescent cells and packaging cell lines for producing thereof
INVENTOR(S): Summerford, Candace; **Gray, John T.**; **Lee, Jeng-Shin**; **Mulligan, Richard C.**
PATENT ASSIGNEE(S): The Children's Medical Center Corporation, USA; President and Fellows of Harvard College
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002059338	A2	20020801	WO 2002-US378	20020107
WO 2002059338	A3	20030724		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2433867	AA	20020801	CA 2002-2433867	20020107
EP 1358342	A2	20031105	EP 2002-714708	20020107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2001-260199P P 20010106
WO 2002-US378 W 20020107

AB Methods of producing retroviral vector particles capable of transducing therapeutic genes into quiescent (non-dividing, resting) cells and methods of gene transfer to quiescent cells comprising infection with a retroviral particle described herein. The present invention is based on inventors' discoveries that retroviral vector particles, which encode the wild-type spleen necrosis virus (SNV) gag-pol gene products, can transfect quiescent cells and do not require a nuclear localization sequence (NLS) in the matrix protein to transfect quiescent cells. The invention relates to novel packaging cell lines useful for generating retroviral vector particles capable of infecting and transducing a DNA sequence of interest into quiescent cells, to construction of such cell lines and to methods of using the particles to introduce transgene into quiescent animal cells (particularly mammalian cells). Sequences required for packaging and reverse transcription can be derived from Moloney leukemia virus (MLV), SNV or other viruses. In particular embodiments, the heterologous envelope protein is the G glycoprotein of vesicular stomatitis virus (VSV G) or the amphotropic envelope of the MLV. The packaging cell lines and viral particles of the present invention can be used in gene therapy or gene replacement to introduce genes into a variety of quiescent cells.

=> D HIS

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FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 15:35:52 ON 21 APR 2005
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L2 6393 S (MULLIGAN, ?)/IN,AU
L3 558398 S (LEE, ?)/IN,AU
L4 627388 S L1 OR L2 OR L3
L5 5 S L1 AND L2 AND L3
L6 2 DUPLICATE REMOVE L5 (3 DUPLICATES REMOVED)

=> S L1 OR L2 OR L3
L7 627388 L1 OR L2 OR L3

=> S (KOTSOPOULOU, ?)/IN,AU
'IN' IS NOT A VALID FIELD CODE
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L8 42 (KOTSOPOULOU, ?)/IN,AU

=> S (KIM, ?)/IN,AU
'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
L9 392484 (KIM, ?)/IN,AU

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L10 744 (KINGSMAN, ?)/IN,AU

=> S (MITROPHANOUS, ?)/IN,AU
'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
L11 137 (MITROPHANOUS, ?)/IN,AU

=> S L8 AND L9 AND L10 AND L11
L12 5 L8 AND L9 AND L10 AND L11

=> DUPLICATE REMOVE L12
DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):N
PROCESSING COMPLETED FOR L12

L13 2 DUPLICATE REMOVE L12 (3 DUPLICATES REMOVED)

=> D IBIB AB L13 1,2

L13 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:781146 CAPLUS
DOCUMENT NUMBER: 135:340191
TITLE: HIV-1 and EIAV derived retroviral vector constructs with codon-optimized gag-pol genes and their uses
INVENTOR(S): **Kingsman, Alan John**; **Kim, Narry**; **Kotsopoulou, Ekaterini**; Rohll, Jonathan; **Mitrophanous, Kyriacos Andreou**
PATENT ASSIGNEE(S): Oxford Biomedica (UK) Ltd., UK
SOURCE: PCT Int. Appl., 201 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001079518	A2	20011025	WO 2001-GB1784	20010418
WO 2001079518	A3	20020516		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2404129	AA	20011025	CA 2001-2404129	20010418
EP 1278878	A2	20030129	EP 2001-921651	20010418
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004508808	T2	20040325	JP 2001-577501	20010418
US 2005042234	A1	20050224	US 2003-258089	20030314
PRIORITY APPLN. INFO.:			GB 2000-9760 A	20000419
			WO 2001-GB1784 W	20010418

AB This invention claims a method of producing a replication defective retrovirus comprising transfecting a producer cell with the following: (i) a retroviral genome; (ii) a nucleotide sequence coding for retroviral gag and pol proteins; and (iii) nucleotide sequences encoding other essential viral packaging components not encoded by the nucleotide sequence of (ii); characterized in that the nucleotide sequence coding for retroviral gag and pol proteins is codon optimized for expression in the producer cell. The invention provides synthetic gag-pol polynucleotide sequences which will not be able to recombine or package viral mRNAs in infected cells. Codons in the region of the gag-pol gene which contains overlapping reading frames encoding gag and pol proteins are not optimized, to ensure efficient expression of the gag and pol proteins. The codon-optimized gag-pol sequences for HIV-1 and EIAV (equine infectious anemia virus) disrupt packaging signals near the 5' end of the gag-pol mRNA and also result in Rev/RRE-independent gag-pol mRNA expression and protein production An example of the invention is an HIV-1 based vector system composed of three plasmids: one expressing codon-optimized gene gag-pol; one expressing VSV-G envelope proteins; and one expressing a 360-nucleotide "wild-type" gag sequence and a splice donor. RNA expression, protein expression, titers, and transduction efficiency of the system were determined A similar vector system based on the non-primate lentivirus EIAV was constructed and characterized; however, sequences in the gag gene required

for packaging EIAV appear to differ from the HIV-1 packaging signal.

L13 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2000240070 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10775623
TITLE: A Rev-independent human immunodeficiency virus type 1 (HIV-1)-based vector that exploits a codon-optimized HIV-1 gag-pol gene.
AUTHOR: **Kotsopoulou E; Kim V N; Kingsman A J; Kingsman S M; Mitrophanous K A**
CORPORATE SOURCE: Retrovirus Molecular Biology Group, Department of Biochemistry, University of Oxford, Oxford OX1 3QU, United Kingdom.
SOURCE: Journal of virology, (2000 May) 74 (10) 4839-52. Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000518
Last Updated on STN: 20000518
Entered Medline: 20000511

AB The human immunodeficiency virus (HIV) genome is AU rich, and this imparts a codon bias that is quite different from the one used by human genes. The codon usage is particularly marked for the gag, pol, and env genes. Interestingly, the expression of these genes is dependent on the presence of the Rev/Rev-responsive element (RRE) regulatory system, even in contexts other than the HIV genome. The Rev dependency has been explained in part by the presence of RNA instability sequences residing in these coding regions. The requirement for Rev also places a limitation on the development of HIV-based vectors, because of the requirement to provide an accessory factor. We have now synthesized a complete codon-optimized HIV-1 gag-pol gene. We show that expression levels are high and that expression is Rev independent. This effect is due to an increase in the amount of gag-pol mRNA. Provision of the RRE in cis did not lower protein or RNA levels or stimulate a Rev response. Furthermore we have used this synthetic gag-pol gene to produce HIV vectors that now lack all of the accessory proteins. These vectors should now be safer than murine leukemia virus-based vectors.

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FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 15:35:52 ON 21 APR 2005
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L3 558398 S (LEE, ?)/IN,AU
L4 627388 S L1 OR L2 OR L3
L5 5 S L1 AND L2 AND L3
L6 2 DUPLICATE REMOVE L5 (3 DUPLICATES REMOVED)
L7 627388 S L1 OR L2 OR L3
L8 42 S (KOTSOPOULOU, ?)/IN,AU
L9 392484 S (KIM, ?)/IN,AU
L10 744 S (KINGSMAN, ?)/IN,AU
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               RETROVIR? OR SIV OR MMV

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L17       9889 L16 AND L7

=> S L16 AND L14
L18       4794 L16 AND L14

=> S L16 AND L15
L19        849 L16 AND L15

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L3       558398 S (LEE, ?)/IN,AU
L4       627388 S L1 OR L2 OR L3
L5            5 S L1 AND L2 AND L3
L6            2 DUPLICATE REMOVE L5 (3 DUPLICATES REMOVED)
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L10         744 S (KINGSMAN, ?)/IN,AU
L11         137 S (MITROPHANOUS, ?)/IN,AU
L12           5 S L8 AND L9 AND L10 AND L11
L13           2 DUPLICATE REMOVE L12 (3 DUPLICATES REMOVED)
L14      393256 S L8 OR L9 OR L10 OR L11
L15      108214 S L7 AND L14
L16      646307 S (HUMAN (S) IMMUNODEFICIENCY (S) VIR?) OR HIV OR LENTIVIR? OR
L17        9889 S L16 AND L7
L18        4794 S L16 AND L14
L19         849 S L16 AND L15

=> S (CODON (S) OPTIMIZ?)
L20       1201 (CODON (S) OPTIMIZ?)

=> S L16 AND L20
L21        241 L16 AND L20

=> S L21 AND L7
L22          5 L21 AND L7

=> DUPLICATE REMOVE L22
DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):N
PROCESSING COMPLETED FOR L22
L23           2 DUPLICATE REMOVE L22 (3 DUPLICATES REMOVED)

=> D IBIB AB L23 1,2

L23  ANSWER 1 OF 2     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:   2003125220     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 12639249
```

TITLE: Characterization and selection of **HIV**-1 subtype C isolates for use in vaccine development.

AUTHOR: Williamson Carolyn; Morris Lynn; Maughan Maureen F; Ping Li-Hua; Dryga Sergey A; Thomas Robin; Reap Elizabeth A; Cilliers Tonie; van Harmelen Joanne; Pascual Alvaro; Ramjee Gita; **Gray Glenda**; Johnston Robert; Karim Salim Abdool; Swanstrom Ronald

CORPORATE SOURCE: Division of Medical Virology, University of Cape Town, Observatory, Cape Town, South Africa 7925.. cwilliam@curie.uct.ac.za

CONTRACT NUMBER: AI46023 (NIAID)
P30-AI50410 (NIAID)

SOURCE: AIDS research and human retroviruses, (2003 Feb) 19 (2) 133-44.
Journal code: 8709376. ISSN: 0889-2229.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; AIDS

OTHER SOURCE: GENBANK-AF543896; GENBANK-AF543897; GENBANK-AF543898; GENBANK-AF543899; GENBANK-AF543900; GENBANK-AF543901; GENBANK-AF543902; GENBANK-AF543903; GENBANK-AF543904; GENBANK-AF543905; GENBANK-AF543906; GENBANK-AF543907; GENBANK-AF543908; GENBANK-AF543909; GENBANK-AF543910; GENBANK-AF543911; GENBANK-AF543912; GENBANK-AF543913; GENBANK-AF543914; GENBANK-AF543915; GENBANK-AF543916; GENBANK-AF543917; GENBANK-AF543918; GENBANK-AF543919; GENBANK-AF543920; GENBANK-AF543921; GENBANK-AF543922; GENBANK-AF543923; GENBANK-AF543924; GENBANK-AF543925; GENBANK-AF543926; GENBANK-AF543927; GENBANK-AF543928; GENBANK-AF543929; GENBANK-AF543930; GENBANK-AF543931; GENBANK-AF543932; GENBANK-AF543933; GENBANK-AF543934; GENBANK-AF543935; GENBANK-AF543936; GENBANK-AF543937; GENBANK-AF543938; GENBANK-AF543939; GENBANK-AF543940; GENBANK-AF543941; GENBANK-AF543942; GENBANK-AF543943; GENBANK-AF543944; GENBANK-AF543945; GENBANK-AF543946; GENBANK-AF543947; GENBANK-AF543948; GENBANK-AF543949; GENBANK-AF543950; GENBANK-AF543951; GENBANK-AF543952; GENBANK-AF543953; GENBANK-AF543954; GENBANK-AF543955; GENBANK-AF543956; GENBANK-AF543957; GENBANK-AF543958; GENBANK-AF543959; GENBANK-AF543960; GENBANK-AF543961; GENBANK-AF543962; GENBANK-AF543963; GENBANK-AF543964; GENBANK-AF543965; GENBANK-AF543966; GENBANK-AF543967; GENBANK-AF543968; GENBANK-AF543969; GENBANK-AF543970; GENBANK-AF543971; GENBANK-AF543972; GENBANK-AF543973; GENBANK-AF543974; GENBANK-AF543975; GENBANK-AF543976; GENBANK-AF543977; GENBANK-AF543978; GENBANK-AF543979; GENBANK-AF543980; GENBANK-AF543981; GENBANK-AF543982; GENBANK-AF543983; GENBANK-AF543984; GENBANK-AF543985; GENBANK-AF543986; GENBANK-AF543987; GENBANK-AF543988; GENBANK-AF543989; GENBANK-AF543990; GENBANK-AF543991; GENBANK-AF543992; GENBANK-AF543993; GENBANK-AF543994; GENBANK-AF543995; GENBANK-AF543996; GENBANK-AF543997; GENBANK-AF543998; GENBANK-AF543999; GENBANK-AF544000; GENBANK-AF544001; GENBANK-AF544002; GENBANK-AF544003; GENBANK-AF544004; GENBANK-AF544005; GENBANK-AF544006; GENBANK-AF544007; GENBANK-AF544008; GENBANK-AF544009; GENBANK-AF544010

ENTRY MONTH: 200305

ENTRY DATE: Entered STN: 20030318
Last Updated on STN: 20030520
Entered Medline: 20030519

AB **HIV**-1 genetic diversity among circulating strains presents a

major challenge for **HIV**-1 vaccine development, particularly for developing countries where less sequence information is available. To identify representative viruses for inclusion in candidate vaccines targeted for South Africa, we applied an efficient sequence survey strategy to samples from recently and chronically infected persons residing in potential vaccine trial sites. All 111 sequences were subtype C, including 30 partial gag, 26 partial pol, 27 V2-V3 env, and 28 V5-partial gp41 sequences. Of the 10 viruses cultured from recently infected individuals, 9 were R5 and 1 was R5X4. Two isolates, Du151 and Du422, collected within 2 months of infection, were selected as vaccine strains on the basis of their amino acid similarity to a derived South African consensus sequence The selection of recently transmitted R5 isolates for vaccine design may provide an advantage in a subtype C R5-dominant epidemic. The full-length Du422 gag and Du151 pol and env genes were cloned into the Venezuelan equine encephalitis (VEE) replicon particle (VRP) expression system. Du422 Gag protein expressed from the VRP accumulated to a high level and was immunogenic as demonstrated by cytotoxic T lymphocyte responses in mice vaccinated with gag-VRPs. **Optimization** of **codon** use for VRP expression in human cells did not enhance expression of the gag gene. The cloned Du151 env gene encoded a functional protein as demonstrated by fusion of VRP-infected cells with cells expressing CD4 and CCR5. Genes identified in this study have been incorporated into the VEE VRP candidate vaccines targeted for clinical trial in South Africa.

L23 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:191238 CAPLUS
DOCUMENT NUMBER: 132:232375
TITLE: Packaging cell lines for generation of **retroviral** vector particles free of accessory proteins
INVENTOR(S): **Gray, John T.; Mulligan, Richard C.**
PATENT ASSIGNEE(S): The Children's Medical Center Corp., USA
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000015819	A1	20000323	WO 1999-US20675		19990910
W: AU, CA, JP					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
AU 9961396	A1	20000403	AU 1999-61396		19990910
PRIORITY APPLN. INFO.:			US 1998-100022P	P	19980911
			US 1998-100063P	P	19980912
			WO 1999-US20675	W	19990910

AB Novel packaging cell lines useful for generating viral accessory protein independent **HIV**-derived **retroviral** vector particles, methods of constructing such packaging cell lines and methods of using the viral accessory protein independent **HIV**-derived **retroviral** vector particles are disclosed. The cell lines carry the **retroviral** gag-pol and env genes with **codon** usage **optimized** for expression in the host cell and the nucleic acid to be packaged under the control of **retroviral** cis-acting sequences for packaging, reverse transcription, and integration. The gag-pol and env genes may be from different viruses and the gag and pol genes may be separated and from different viruses. Genes for accessory proteins and certain cis-acting elements (constitutive transport elements) are absent.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> D HIS

     (FILE 'HOME' ENTERED AT 15:35:40 ON 21 APR 2005)

     FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 15:35:52 ON 21 APR 2005
L1         63641 S (GRAY, ?)/IN,AU
L2          6393 S (MULLIGAN, ?)/IN,AU
L3        558398 S (LEE, ?)/IN,AU
L4        627388 S L1 OR L2 OR L3
L5             5 S L1 AND L2 AND L3
L6             2 DUPLICATE REMOVE L5 (3 DUPLICATES REMOVED)
L7        627388 S L1 OR L2 OR L3
L8            42 S (KOTSOPOULOU, ?)/IN,AU
L9        392484 S (KIM, ?)/IN,AU
L10          744 S (KINGSMAN, ?)/IN,AU
L11          137 S (MITROPHANOUS, ?)/IN,AU
L12            5 S L8 AND L9 AND L10 AND L11
L13            2 DUPLICATE REMOVE L12 (3 DUPLICATES REMOVED)
L14       393256 S L8 OR L9 OR L10 OR L11
L15       108214 S L7 AND L14
L16       646307 S (HUMAN (S) IMMUNODEFICIENCY (S) VIR?) OR HIV OR LENTIVIR? OR
L17         9889 S L16 AND L7
L18         4794 S L16 AND L14
L19          849 S L16 AND L15
L20         1201 S (CODON (S) OPTIMIZ?)
L21          241 S L16 AND L20
L22            5 S L21 AND L7
L23            2 DUPLICATE REMOVE L22 (3 DUPLICATES REMOVED)

=> S L21 AND L14
L24           14 L21 AND L14

=> DUPLICATE REMOVE L24
DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):N
PROCESSING COMPLETED FOR L24
L25            8 DUPLICATE REMOVE L24 (6 DUPLICATES REMOVED)

=> D IBIB AB L25 1-8

L25  ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:1078  CAPLUS
DOCUMENT NUMBER:          142:79860
TITLE:                    Use of retroviral vectors expressing
                          RARβ2 and/or an agonist thereof for neurite
                          regeneration in treating nerve injury
INVENTOR(S):              Wong, Liang Fong; Mazarakis, Nicholas; Kingsman,
                          Alan; McMahon, Stephen; Maden, Malcolm
PATENT ASSIGNEE(S):       UK
SOURCE:                   U.S. Pat. Appl. Publ., 196 pp., Cont.-in-part of U.S.
                          Ser. No. 716,725.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   6
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     US 2004266715         A1    20041230    US 2004-838906          20040503
```

WO 2000057900 A2 20001005 WO 2000-GB1211 20000330
WO 2000057900 A3 20010215
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
WO 2001075135 A1 20011011 WO 2001-GB1478 20010330
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
WO 2002036170 A2 20020510 WO 2001-GB4866 20011102
WO 2002036170 A3 20020822
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2003053991 A1 20030320 US 2002-239804 20020923
US 2004071675 A1 20040415 US 2003-429608 20030505
WO 2004031390 A1 20040415 WO 2003-GB4260 20031003
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2004076613 A1 20040422 US 2003-716725 20031119

PRIORITY APPLN. INFO.:

GB 1999-7461	A	19990331
WO 2000-GB1211	W	20000330
GB 2000-24300	A	20001004
GB 2000-26943	A	20001103
GB 2001-2339	A	20010130
WO 2001-GB1478	W	20010330
GB 2001-22238	A	20010914
WO 2001-GB4866	A2	20011102
US 2002-937716	A2	20020701
US 2002-239804	A2	20020923
GB 2002-23076	A	20021004
GB 2002-28314	A	20021204
US 2003-429608	A2	20030505
GB 2003-18213	A	20030804
WO 2003-GB4260	A2	20031003
US 2003-716725	A2	20031119

AB The present invention relates to the use of retinoic acid receptor

RAR-β2 and/or an agonist thereof in the preparation of a medicament to cause neurite development, neurite growth and/or neurite regeneration. The present invention is based on the finding that it is possible to cause neurite development, such as neurite outgrowth and/or neurite regeneration, by using RAR2 and/or an agonist thereof, and that RAR2 may be introduced into neuronal cells using **retroviral** vectors based on **lentiviral** vectors. In another aspect, the present invention relates to a method of treating a neurol. disorder such as a nerve injury comprising administering a pharmacol. active amount of an RAR2 receptor, and/or an agonist thereof, wherein said agonist is RA and/or CD2019. Provided sequence of plasmid vectors of invention.

L25 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:473147 CAPLUS
DOCUMENT NUMBER: 139:48169
TITLE: Packaging cells regulated by tetracycline-sodium butyrate system for producing high titer pseudotyped viral vectors, specifically equine infectious anemia virus vectors
INVENTOR(S): Olsen, John C.; **Mitrophanous, Kyriacos Andreou**; Rohll, Jonathan; **Kingsman, Alan John**; Ellard, Fiona Margaret
PATENT ASSIGNEE(S): Oxford Biomedica (UK) Limited, USA
SOURCE: U.S. Pat. Appl. Publ., 98 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003113898	A1	20030619	US 2002-134643		20020430
CA 2344208	AA	20021030	CA 2001-2344208		20010430
PRIORITY APPLN. INFO.:			CA 2001-2344208	A	20010430
			US 2001-287048P	P	20010430

AB The present invention relates to methods for producing pseudotyped viral vectors with a broad host range which can be produced at sufficient titers in packaging and/or stable producer cell lines. Most specifically, the invention relates to the generation of pseudotyped **retroviral** vectors having vesicular stomatitis virus-G protein (VSV-G) as the membrane-associated viral envelope protein. The present invention describes a novel system for producing high titer vectors wherein the production of the vectors is activated by doxycycline, but only after an initial stimulus with sodium butyrate--full activation is not observed in the presence of doxycycline alone. However following an initial treatment with sodium butyrate, the system can be maintained in an active state by supplying doxycycline alone. The producer cell comprises: (i) a first nucleotide sequence (NS) encoding a toxic viral envelope protein operably linked to a promoter; wherein the promoter is operably linked to at least one copy of a TRE (tetracycline-responsive element); (ii) a second NS encoding a tetracycline modulator; (iii) a third NS encoding a **retrovirus** nucleocapsid protein; and (iv) a fourth NS comprising a **retroviral** sequence capable of being encapsidated in the nucleocapsid protein such that the **retroviral** vector particle titer obtainable from the producer cell is regulatable by tetracycline and an initial stimulus with sodium butyrate or functional analogs thereof. The present invention also relates to **lentiviral** vectors, in particular those derived from equine infectious anemia virus (EIAV), useful in gene delivery to non-dividing and dividing cells. Thus, our invention relates to a method for making a producer cell capable of making EIAV vector efficiently and safely and in an REV/RRE independent manner. The inventors found that woodchuck hepatitis virus (WHV) post-transcriptional regulatory element

(PRE) can substitute for the REV/RRE in the EIAV vector system.

L25 ANSWER 3 OF 8 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2003202646 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12679787
TITLE: Continuous high-titer **HIV**-1 vector production.
AUTHOR: Ikeda Yasuhiro; Takeuchi Yasuhiro; Martin Francisco; Cosset Francois-Loic; **Mitrophanous Kyriacos**; Collins Mary
CORPORATE SOURCE: Department of Immunology and Molecular Pathology, Windeyer Institute, University College London, 46 Cleveland St., London W1T 4JF, UK.
SOURCE: Nature biotechnology, (2003 May) 21 (5) 569-72. Electronic Publication: 2003-04-07.
Journal code: 9604648. ISSN: 1087-0156.
PUB. COUNTRY: United States
DOCUMENT TYPE: (EVALUATION STUDIES)
Report; (TECHNICAL REPORT)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 20030501
Last Updated on STN: 20040106
Entered Medline: 20040105

AB **Human immunodeficiency virus** type 1 (**HIV**-1)-based vectors are currently made by transient transfection, or using packaging cell lines in which expression of **HIV**-1 Gag and Pol proteins is induced. Continuous vector production by cells in which **HIV**-1 Gag-Pol is stably expressed would allow rapid and reproducible generation of large vector batches. However, attempts to make stable **HIV**-1 packaging cells by transfection of plasmids encoding **HIV**-1 Gag-Pol have resulted in cells which secrete only low levels of p24 antigen (20-80 ng/ml), possibly because of the cytotoxicity of **HIV**-1 protease. Infection of cells with **HIV**-1 can result in stable virus production; cell clones that produce up to 1,000 ng/ml secreted p24 antigen have been described. Here we report that expression of **HIV**-1 Gag-Pol by a murine leukemia virus (MLV) vector allows constitutive, long-term, high-level (up to 850 ng/ml p24) expression of **HIV**-1 Gag. Stable packaging cells were constructed using **codon-optimized HIV**-1 Gag-Pol and envelope proteins of gammaretroviruses; these producer cells could make up to 10(7) 293T infectious units (i.u.)/ml (20 293T i.u./cell/day) for at least three months in culture.

L25 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:276168 CAPLUS
DOCUMENT NUMBER: 136:289952
TITLE: **Retroviral** vector system comprising internal ribosome entry for Parkinson's disease gene therapy
INVENTOR(S): **Kingsman, Alan John**; Mazarakis, Nicholas D.; Martin-Rendon, Enca; Azzouz, Mimoun; Rohll, Jonathan
PATENT ASSIGNEE(S): Oxford Biomedica (UK) Limited, UK
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002029065	A2	20020411	WO 2001-GB4433	20011005
WO 2002029065	A3	20021227		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2424738	AA	20020411	CA 2001-2424738	20011005
AU 2001092093	A5	20020415	AU 2001-92093	20011005
EP 1337655	A2	20030827	EP 2001-972317	20011005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004520016	T2	20040708	JP 2002-532634	20011005
US 2004013648	A1	20040122	US 2003-408456	20030407
US 2005002907	A1	20050106	US 2004-873573	20040621
PRIORITY APPLN. INFO.:			GB 2000-24550 A	20001006
			WO 2001-GB4433 W	20011005
			US 2003-408456 A2	20030407

AB The present invention relates to **retroviral** vector for treating a neurodegenerative disorder or Parkinson's disease. In particular the present invention relates to a **retroviral** vector lacking the rev responsive element and comprising two or more NOI (nucleotide sequence of interest) operably linked by one or more Internal Ribosome Entry Site(s). The said **lentiviral** vector comprise sequences encoding tyrosine hydroxylase, GTP-cyclohydrolase I or optionally aromatic amino acid Dopa decarboxylase. The invention also relates to transiently expression of NOI from bicistronic and tricistronic cassettes in heterologous human cells. EIAV-TRIC vectors uses for correcting the 6-hydroxydopamine (6-OHDA) and 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) primate model of Parkinson's disease.

L25 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:781146 CAPLUS
DOCUMENT NUMBER: 135:340191
TITLE: **HIV**-1 and EIAV derived **retroviral** vector constructs with **codon-optimized** gag-pol genes and their uses
INVENTOR(S): **Kingsman, Alan John**; **Kim, Narry**; **Kotsopoulou, Ekaterini**; Rohll, Jonathan; **Mitrophanous, Kyriacos Andreou**
PATENT ASSIGNEE(S): Oxford Biomedica (UK) Ltd., UK
SOURCE: PCT Int. Appl., 201 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001079518	A2	20011025	WO 2001-GB1784	20010418
WO 2001079518	A3	20020516		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2404129	AA	20011025	CA 2001-2404129		20010418
EP 1278878	A2	20030129	EP 2001-921651		20010418
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004508808	T2	20040325	JP 2001-577501		20010418
US 2005042234	A1	20050224	US 2003-258089		20030314
PRIORITY APPLN. INFO.:			GB 2000-9760	A	20000419
			WO 2001-GB1784	W	20010418

AB This invention claims a method of producing a replication defective **retrovirus** comprising transfecting a producer cell with the following: (i) a **retroviral** genome; (ii) a nucleotide sequence coding for **retroviral** gag and pol proteins; and (iii) nucleotide sequences encoding other essential viral packaging components not encoded by the nucleotide sequence of (ii); characterized in that the nucleotide sequence coding for **retroviral** gag and pol proteins is **codon optimized** for expression in the producer cell. The invention provides synthetic gag-pol polynucleotide sequences which will not be able to recombine or package viral mRNAs in infected cells. Codons in the region of the gag-pol gene which contains overlapping reading frames encoding gag and pol proteins are not optimized, to ensure efficient expression of the gag and pol proteins. The **codon-optimized** gag-pol sequences for **HIV**-1 and EIAV (equine infectious anemia virus) disrupt packaging signals near the 5' end of the gag-pol mRNA and also result in Rev/RRE-independent gag-pol mRNA expression and protein production An example of the invention is an **HIV**-1 based vector system composed of three plasmids: one expressing **codon-optimized** gene gag-pol; one expressing VSV-G envelope proteins; and one expressing a 360-nucleotide "wild-type" gag sequence and a splice donor. RNA expression, protein expression, titers, and transduction efficiency of the system were determined A similar vector system based on the non-primate **lentivirus** EIAV was constructed and characterized; however, sequences in the gag gene required for packaging EIAV appear to differ from the **HIV**-1 packaging signal.

L25 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2000:666894 CAPLUS
DOCUMENT NUMBER:	133:262244
TITLE:	System for producing external guide sequence-encoding viral vectors for treatment of viral infections
INVENTOR(S):	Uden, Mark; **Mitrophanous, Kyriacos**
PATENT ASSIGNEE(S):	Oxford Biomedica (UK) Limited, UK
SOURCE:	PCT Int. Appl., 62 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000055341	A1	20000921	WO 2000-GB1002	20000317
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
GB 2363794	A1	20020109	GB 2001-22683	20000317
EP 1192265	A1	20020403	EP 2000-911067	20000317

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

JP 2002538829	T2	20021119	JP 2000-605758		20000317
US 6783981	B1	20040831	US 2001-936572		20011211
PRIORITY APPLN. INFO.:			GB 1999-6177	A	19990317
			WO 2000-GB1002	W	20000317

AB A viral vector production system is provided which system comprises: (i) a viral genome comprising at least one first nucleotide sequence encoding a gene product capable of binding to and effecting the cleavage, directly or indirectly, of a second nucleotide sequence, or transcription product thereof, encoding a viral polypeptide required for the assembly of viral particles; (ii) a third nucleotide sequence encoding said viral polypeptide required for the assembly of the viral genome into viral particles, which third nucleotide sequence has a different nucleotide sequence to the second nucleotide sequence such that said third nucleotide sequence, or transcription product thereof, is resistant to cleavage directed by said gene product; wherein at least one of the gene products is an external guide sequence (EGS) capable of binding to and effecting the cleavage by RNase P of the second nucleotide sequence. The viral vector production system may be used to produce viral particles for use in treating or preventing viral infection. Thus, a system for producing **HIV** particles encoding EGSs (and, optionally, anti-**HIV** ribozymes or antisense RNAs) includes an **HIV** genome encoding the EGS and nucleotide constructs encoding the components required for packaging the viral genome in the producer cell. In contrast to the prior art, although the packaging components have substantially the same amino acid sequence as the corresponding components of the target virus, the inhibitory RNA mols. do not affect production of the viral particles in the producer cells because the nucleotide sequence of the packaging components used in the viral system have been modified to prevent the inhibitory RNA mols. from effecting cleavage or degradation of the RNA transcripts produced from the constructs.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 7 OF 8 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER:	2000240070 MEDLINE
DOCUMENT NUMBER:	PubMed ID: 10775623
TITLE:	A Rev-independent **human immunodeficiency virus** type 1 (**HIV**-1)-based vector that exploits a **codon-optimized HIV** -1 gag-pol gene.
AUTHOR:	**Kotsopoulou E; Kim V N; Kingsman A J; Kingsman S M; Mitrophanous K A**
CORPORATE SOURCE:	Retrovirus Molecular Biology Group, Department of Biochemistry, University of Oxford, Oxford OX1 3QU, United Kingdom.
SOURCE:	Journal of virology, (2000 May) 74 (10) 4839-52. Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY:	United States
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals; AIDS
ENTRY MONTH:	200005
ENTRY DATE:	Entered STN: 20000518 Last Updated on STN: 20000518 Entered Medline: 20000511

AB The **human immunodeficiency virus** (**HIV**) genome is AU rich, and this imparts a codon bias that is quite different from the one used by **human** genes. The codon usage is particularly marked for the gag, pol, and env genes. Interestingly, the expression of these genes is dependent on the presence of the Rev/Rev-responsive element (RRE) regulatory system, even in

contexts other than the **HIV** genome. The Rev dependency has been explained in part by the presence of RNA instability sequences residing in these coding regions. The requirement for Rev also places a limitation on the development of **HIV**-based vectors, because of the requirement to provide an accessory factor. We have now synthesized a complete **codon-optimized HIV**-1 gag-pol gene. We show that expression levels are high and that expression is Rev independent. This effect is due to an increase in the amount of gag-pol mRNA. Provision of the RRE in cis did not lower protein or RNA levels or stimulate a Rev response. Furthermore we have used this synthetic gag-pol gene to produce **HIV** vectors that now lack all of the accessory proteins. These vectors should now be safer than murine leukemia virus-based vectors.

L25 ANSWER 8 OF 8 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:431853 BIOSIS
DOCUMENT NUMBER: PREV200000431853
TITLE: Characterization of the equine infectious anaemia virus S2 protein.
AUTHOR(S): Yoon, Soonsang; **Kingsman, Susan M.**; **Kingsman, Alan J.**; Wilson, Stuart A.; **Mitrophanous, Kyriacos A.** [Reprint author]
CORPORATE SOURCE: Oxford Biomedica (UK) Ltd, Oxford Science Park, Oxford, OX4 4GA, UK
SOURCE: Journal of General Virology, (September, 2000) Vol. 81, No. 9, pp. 2189-2194. print.
CODEN: JGVIAY. ISSN: 0022-1317.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Oct 2000
Last Updated on STN: 10 Jan 2002

AB S2 is an accessory protein of equine infectious anaemia virus (EIAV), the function of which is unknown. In order to gain insight into the function of S2, the intracellular localization of the protein, its interaction with viral proteins and its incorporation into viral particles have been investigated. Immunolocalization of S2 revealed punctuate staining in the cytoplasm and the S2 protein coprecipitated with the EIAV Gag precursor. Despite overexpression of S2 through the use of a **codon-optimized** sequence, there was no preferential association of S2 with EIAV particles. These data suggest that S2 may function to organize the Gag protein during particle assembly in the cytoplasm but that it is unlikely to be involved in the early stages of the virus life-cycle.

=> D HIS

(FILE 'HOME' ENTERED AT 15:35:40 ON 21 APR 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 15:35:52 ON 21 APR 2005

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L1        63641 S (GRAY, ?)/IN,AU
L2         6393 S (MULLIGAN, ?)/IN,AU
L3       558398 S (LEE, ?)/IN,AU
L4       627388 S L1 OR L2 OR L3
L5            5 S L1 AND L2 AND L3
L6            2 DUPLICATE REMOVE L5 (3 DUPLICATES REMOVED)
L7       627388 S L1 OR L2 OR L3
L8           42 S (KOTSOPOULOU, ?)/IN,AU
L9       392484 S (KIM, ?)/IN,AU
L10         744 S (KINGSMAN, ?)/IN,AU
L11         137 S (MITROPHANOUS, ?)/IN,AU
L12           5 S L8 AND L9 AND L10 AND L11
L13           2 DUPLICATE REMOVE L12 (3 DUPLICATES REMOVED)
L14      393256 S L8 OR L9 OR L10 OR L11
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L15      108214 S L7 AND L14
L16      646307 S (HUMAN (S) IMMUNODEFICIENCY (S) VIR?) OR HIV OR LENTIVIR? OR
L17        9889 S L16 AND L7
L18        4794 S L16 AND L14
L19         849 S L16 AND L15
L20        1201 S (CODON (S) OPTIMIZ?)
L21         241 S L16 AND L20
L22           5 S L21 AND L7
L23           2 DUPLICATE REMOVE L22 (3 DUPLICATES REMOVED)
L24          14 S L21 AND L14
L25           8 DUPLICATE REMOVE L24 (6 DUPLICATES REMOVED)

=> S (GAGPOL OR GAG OR POL)
L26      65288 (GAGPOL OR GAG OR POL)

=> S L26 AND L20
L27        142 L26 AND L20

=> S L27 AND (L7 OR L14)
L28         20 L27 AND (L7 OR L14)

=> S L28 NOT (L22 OR L24)
L29          2 L28 NOT (L22 OR L24)

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DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):N
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L30          1 DUPLICATE REMOVE L29 (1 DUPLICATE REMOVED)

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L30 ANSWER 1 OF 1     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:   2001021699     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 10950976
TITLE:              Characterization of the equine infectious anaemia virus S2
                    protein.
AUTHOR:             Yoon S; Kingsman S M; Kingsman A J;
                    Wilson S A; Mitrophanous K A
CORPORATE SOURCE:   Retrovirus Molecular Biology Group, Department of
                    Biochemistry, University of Oxford, South Parks Road,
                    Oxford OX1 3QU, UK.
SOURCE:             Journal of general virology, (2000 Sep) 81 (Pt 9) 2189-94.
                    Journal code: 0077340. ISSN: 0022-1317.
PUB. COUNTRY:       ENGLAND: United Kingdom
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200011
ENTRY DATE:         Entered STN: 20010322
                    Last Updated on STN: 20020212
                    Entered Medline: 20001109
AB   S2 is an accessory protein of equine infectious anaemia virus (EIAV), the
     function of which is unknown. In order to gain insight into the function
     of S2, the intracellular localization of the protein, its interaction with
     viral proteins and its incorporation into viral particles have been
     investigated. Immunolocalization of S2 revealed punctate staining in the
     cytoplasm and the S2 protein co-precipitated with the EIAV Gag
     precursor. Despite overexpression of S2 through the use of a
     codon-optimized sequence, there was no preferential
     association of S2 with EIAV particles. These data suggest that S2 may
     function to organize the Gag protein during particle assembly in
     the cytoplasm but that it is unlikely to be involved in the early stages
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of the virus life-cycle.

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=> D HIS

     (FILE 'HOME' ENTERED AT 15:35:40 ON 21 APR 2005)

     FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 15:35:52 ON 21 APR 2005
L1         63641 S (GRAY, ?)/IN,AU
L2          6393 S (MULLIGAN, ?)/IN,AU
L3        558398 S (LEE, ?)/IN,AU
L4        627388 S L1 OR L2 OR L3
L5             5 S L1 AND L2 AND L3
L6             2 DUPLICATE REMOVE L5 (3 DUPLICATES REMOVED)
L7        627388 S L1 OR L2 OR L3
L8            42 S (KOTSOPOULOU, ?)/IN,AU
L9        392484 S (KIM, ?)/IN,AU
L10          744 S (KINGSMAN, ?)/IN,AU
L11          137 S (MITROPHANOUS, ?)/IN,AU
L12            5 S L8 AND L9 AND L10 AND L11
L13            2 DUPLICATE REMOVE L12 (3 DUPLICATES REMOVED)
L14       393256 S L8 OR L9 OR L10 OR L11
L15       108214 S L7 AND L14
L16       646307 S (HUMAN (S) IMMUNODEFICIENCY (S) VIR?) OR HIV OR LENTIVIR? OR
L17         9889 S L16 AND L7
L18         4794 S L16 AND L14
L19          849 S L16 AND L15
L20         1201 S (CODON (S) OPTIMIZ?)
L21          241 S L16 AND L20
L22            5 S L21 AND L7
L23            2 DUPLICATE REMOVE L22 (3 DUPLICATES REMOVED)
L24           14 S L21 AND L14
L25            8 DUPLICATE REMOVE L24 (6 DUPLICATES REMOVED)
L26        65288 S (GAGPOL OR GAG OR POL)
L27          142 S L26 AND L20
L28           20 S L27 AND (L7 OR L14)
L29            2 S L28 NOT (L22 OR L24)
L30            1 DUPLICATE REMOVE L29 (1 DUPLICATE REMOVED)

=> S (LACK? OR DEVOID? OR DEFICIENT? OR "without")
L31     4339034 (LACK? OR DEVOID? OR DEFICIENT? OR "WITHOUT")

=> s ("CTE" or "CTEs" OR (CONSTITUTIVE (S) TRANSPORT (S) ELEMENT))
L32        2584 ("CTE" OR "CTES" OR (CONSTITUTIVE (S) TRANSPORT (S) ELEMENT))

=> S ("RRE" or "REV" or (rev (s) response (s) element?)
UNMATCHED LEFT PARENTHESIS '("RRE"'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> S ("RRE" or "REV" or (rev (s) response (s) element?))
L33       34022 ("RRE" OR "REV" OR (REV (S) RESPONSE (S) ELEMENT?))

=> s ("CTE" or "CTEs" OR (CONSTITUTIVE (S) TRANSPORT (S) ELEMENT?))
L34        2598 ("CTE" OR "CTES" OR (CONSTITUTIVE (S) TRANSPORT (S) ELEMENT?))

=> d his

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L1         63641 S (GRAY, ?)/IN,AU
L2          6393 S (MULLIGAN, ?)/IN,AU
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L3        558398 S (LEE, ?)/IN,AU
L4        627388 S L1 OR L2 OR L3
L5             5 S L1 AND L2 AND L3
L6             2 DUPLICATE REMOVE L5 (3 DUPLICATES REMOVED)
L7        627388 S L1 OR L2 OR L3
L8            42 S (KOTSOPOULOU, ?)/IN,AU
L9        392484 S (KIM, ?)/IN,AU
L10          744 S (KINGSMAN, ?)/IN,AU
L11          137 S (MITROPHANOUS, ?)/IN,AU
L12            5 S L8 AND L9 AND L10 AND L11
L13            2 DUPLICATE REMOVE L12 (3 DUPLICATES REMOVED)
L14       393256 S L8 OR L9 OR L10 OR L11
L15       108214 S L7 AND L14
L16       646307 S (HUMAN (S) IMMUNODEFICIENCY (S) VIR?) OR HIV OR LENTIVIR? OR
L17         9889 S L16 AND L7
L18         4794 S L16 AND L14
L19          849 S L16 AND L15
L20         1201 S (CODON (S) OPTIMIZ?)
L21          241 S L16 AND L20
L22            5 S L21 AND L7
L23            2 DUPLICATE REMOVE L22 (3 DUPLICATES REMOVED)
L24           14 S L21 AND L14
L25            8 DUPLICATE REMOVE L24 (6 DUPLICATES REMOVED)
L26        65288 S (GAGPOL OR GAG OR POL)
L27          142 S L26 AND L20
L28           20 S L27 AND (L7 OR L14)
L29            2 S L28 NOT (L22 OR L24)
L30            1 DUPLICATE REMOVE L29 (1 DUPLICATE REMOVED)
L31      4339034 S (LACK? OR DEVOID? OR DEFICIENT? OR "WITHOUT")
L32         2584 S ("CTE" OR "CTES" OR (CONSTITUTIVE (S) TRANSPORT (S) ELEMENT))
L33        34022 S ("RRE" OR "REV" OR (REV (S) RESPONSE (S) ELEMENT?))
L34         2598 S ("CTE" OR "CTES" OR (CONSTITUTIVE (S) TRANSPORT (S) ELEMENT?)

=> s l33 or l34
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=> s l31 (s) l35
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=> s l36 and l16
L37         428 L36 AND L16

=> s l37 and l20
L38           5 L37 AND L20

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DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L38
L39           2 DUPLICATE REMOVE L38 (3 DUPLICATES REMOVED)

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L39  ANSWER 1 OF 2     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:    2003456252     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 14517067
TITLE:               Novel engineered HIV-1 East African Clade-A gp160
                     plasmid construct induces strong humoral and cell-mediated
                     immune responses in vivo.
AUTHOR:              Muthumani Karuppiah; Zhang Donghui; Dayes Nathanael S;
                     Hwang Daniel S; Calarota Sandra A; Choo Andrew Y; Boyer
                     Jean D; Weiner David B
CORPORATE SOURCE:    Department of Pathology and Laboratory Medicine, University
```

of Pennsylvania, Philadelphia, PA 19104, USA.
SOURCE: Virology, (2003 Sep 15) 314 (1) 134-46.
Journal code: 0110674. ISSN: 0042-6822.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200311
ENTRY DATE: Entered STN: 20031001
Last Updated on STN: 20031104
Entered Medline: 20031103

AB **HIV**-1 sequences are highly diverse due to the inaccuracy of the viral reverse transcriptase. This diversity has been studied and used to categorize **HIV** isolates into subtypes or clades, which are geographically distinct. To develop effective vaccines against **HIV**-1, immunogens representing different subtypes may be important for induction of cross-protective immunity, but little data exist describing and comparing the immunogenicity induced by different subtype-based vaccines. This issue is further complicated by poor expression of **HIV** structural antigens due to rev dependence. One costly approach is to **codon optimize** each subtype construct to be examined. Interestingly, cis-acting transcriptional elements (CTE) can also by pass rev restriction by a rev independent export pathway. We reasoned that rev+CTE constructs might have advantages for such expression studies. A subtype A envelope sequence from a viral isolate from east Africa was cloned into a eukaryotic expression vector under the control of the CMV-IE promoter. The utility of inclusion of the Mason-Pfizer monkey virus (MPV)-**CTE** with/**without** **rev** for driving envelope expression and immunogenicity was examined. Expression of envelope (gp120) was confirmed by immunoblot analysis and by pseudotype virus infectivity assays. The presence of rev and the CTE together increased envelope expression and viral infection. Furthermore the CTE+rev construct was significantly more immunogenic then CTE alone vector. Isotype analysis and cytokine profiles showed strong Th1 response in plasmid-immunized mice, which also demonstrated the superior nature of the rev+CTE construct. These responses were of similar or greater magnitude to a **codon-optimized** construct. The resulting cellular immune responses were highly cross-reactive with a **HIV**-1 envelope subtype B antigen. This study suggests a simple strategy for improving the expression and immunogenicity of **HIV** subtype-specific envelope antigens as plasmid or vector-borne immunogens.

L39 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:276168 CAPLUS
DOCUMENT NUMBER: 136:289952
TITLE: **Retroviral** vector system comprising internal ribosome entry for Parkinson's disease gene therapy
INVENTOR(S): Kingsman, Alan John; Mazarakis, Nicholas D.; Martin-Rendon, Enca; Azzouz, Mimoun; Rohll, Jonathan
PATENT ASSIGNEE(S): Oxford Biomedica (UK) Limited, UK
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002029065	A2	20020411	WO 2001-GB4433	20011005
WO 2002029065	A3	20021227		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2424738	AA	20020411	CA 2001-2424738		20011005
AU 2001092093	A5	20020415	AU 2001-92093		20011005
EP 1337655	A2	20030827	EP 2001-972317		20011005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004520016	T2	20040708	JP 2002-532634		20011005
US 2004013648	A1	20040122	US 2003-408456		20030407
US 2005002907	A1	20050106	US 2004-873573		20040621
PRIORITY APPLN. INFO.:			GB 2000-24550	A	20001006
			WO 2001-GB4433	W	20011005
			US 2003-408456	A2	20030407

AB The present invention relates to **retroviral** vector for treating a neurodegenerative disorder or Parkinson's disease. In particular the present invention relates to a **retroviral** vector **lacking** the **rev** responsive element and comprising two or more NOI (nucleotide sequence of interest) operably linked by one or more Internal Ribosome Entry Site(s). The said **lentiviral** vector comprise sequences encoding tyrosine hydroxylase, GTP-cyclohydrolase I or optionally aromatic amino acid Dopa decarboxylase. The invention also relates to transiently expression of NOI from bicistronic and tricistronic cassettes in heterologous human cells. EIAV-TRIC vectors uses for correcting the 6-hydroxydopamine (6-OHDA) and 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) primate model of Parkinson's disease.

=> d his

(FILE 'HOME' ENTERED AT 15:35:40 ON 21 APR 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 15:35:52 ON 21 APR 2005

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L2	6393	S (MULLIGAN, ?)/IN,AU
L3	558398	S (LEE, ?)/IN,AU
L4	627388	S L1 OR L2 OR L3
L5	5	S L1 AND L2 AND L3
L6	2	DUPLICATE REMOVE L5 (3 DUPLICATES REMOVED)
L7	627388	S L1 OR L2 OR L3
L8	42	S (KOTSOPOULOU, ?)/IN,AU
L9	392484	S (KIM, ?)/IN,AU
L10	744	S (KINGSMAN, ?)/IN,AU
L11	137	S (MITROPHANOUS, ?)/IN,AU
L12	5	S L8 AND L9 AND L10 AND L11
L13	2	DUPLICATE REMOVE L12 (3 DUPLICATES REMOVED)
L14	393256	S L8 OR L9 OR L10 OR L11
L15	108214	S L7 AND L14
L16	646307	S (HUMAN (S) IMMUNODEFICIENCY (S) VIR?) OR HIV OR LENTIVIR? OR
L17	9889	S L16 AND L7
L18	4794	S L16 AND L14
L19	849	S L16 AND L15
L20	1201	S (CODON (S) OPTIMIZ?)
L21	241	S L16 AND L20
L22	5	S L21 AND L7
L23	2	DUPLICATE REMOVE L22 (3 DUPLICATES REMOVED)
L24	14	S L21 AND L14
L25	8	DUPLICATE REMOVE L24 (6 DUPLICATES REMOVED)
L26	65288	S (GAGPOL OR GAG OR POL)

```
L27         142 S L26 AND L20
L28          20 S L27 AND (L7 OR L14)
L29           2 S L28 NOT (L22 OR L24)
L30           1 DUPLICATE REMOVE L29 (1 DUPLICATE REMOVED)
L31     4339034 S (LACK? OR DEVOID? OR DEFICIENT? OR "WITHOUT")
L32        2584 S ("CTE" OR "CTES" OR (CONSTITUTIVE (S) TRANSPORT (S) ELEMENT))
L33       34022 S ("RRE" OR "REV" OR (REV (S) RESPONSE (S) ELEMENT?))
L34        2598 S ("CTE" OR "CTES" OR (CONSTITUTIVE (S) TRANSPORT (S) ELEMENT?)
L35       36410 S L33 OR L34
L36         870 S L31 (S) L35
L37         428 S L36 AND L16
L38           5 S L37 AND L20
L39           2 DUPLICATE REMOVE L38 (3 DUPLICATES REMOVED)

=> s all (s) accessory (s) (factors or proteins or polypeptides)
L40         171 ALL (S) ACCESSORY (S) (FACTORS OR PROTEINS OR POLYPEPTIDES)

=> s l40 (s) l31
L41          11 L40 (S) L31

=> s l41 and l16
L42           9 L41 AND L16

=> duplicate remove l42
DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L42
L43           3 DUPLICATE REMOVE L42 (6 DUPLICATES REMOVED)

=> d ibib ab l43 1,2,3

L43  ANSWER 1 OF 3     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:   2003353367     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 12885348
TITLE:              Lentivirus-mediated gene transfer and expression
                    in established human tumor antigen-specific cytotoxic T
                    cells and primary unstimulated T cells.
AUTHOR:             Zhou Xianzheng; Cui Yan; Huang Xin; Yu Zhiwei;. Thomas Amy
                    M; Ye Zhaohui; Pardoll Drew M; Jaffee Elizabeth M; Cheng
                    Linzhao
CORPORATE SOURCE:   Division of Immunology and Hematppoiesis, The Sidney Kimmel
                    Comprehensive Cancer Center at Johns Hopkins, Johns Hopkins
                    University School of Medicine, Baltimore, MD 21231, USA..
                    zhoux058@umn.edu
SOURCE:             Human gene therapy, (2003 Jul 20) 14 (11) 1089-105.
                    Journal code: 9008950. ISSN: 1043-0342.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200309
ENTRY DATE:         Entered STN: 20030730
                    Last Updated on STN: 20030928
                    Entered Medline: 20030926
AB   In this report, we evaluated the efficiency of stable gene transfer into
     established CD8(+) human tumor antigen-specific cytotoxic T cell (CTL)
     lines and peripheral blood lymphocytes (PBL) by oncoretroviral and
     lentiviral vectors.  In the oncoretroviral vector, the green
     fluorescent protein (GFP) reporter gene was regulated by the murine stem
     cell virus (MSCV) promoter.  In three human
     immunodeficiency virus type 1 (HIV-1)-based
     lentiviral vectors, the GFP transgene was regulated by either a
     chimeric MSCV/HIV-1 promoter, or cellular promoters from
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human housekeeping genes PGK and EF1 alpha. We found that several lines of proliferating tumor-specific CTL were poorly (=2%) transduced by the oncoretroviral vector that transduced Jurkat T cell line efficiently (=80%). In contrast, three **lentiviral** vectors transduced 38-63% of these proliferating CTL. More interestingly, **all lentiviral** vectors packaged **without** the **HIV**-1 **accessory proteins** transduced human bulk PBL and purified CD4(+) and CD8(+) lymphocyte subsets **without** prior stimulation. Detailed analysis indicated that the **lentiviral** vectors containing the EF1 alpha or PGK ubiquitous promoter can transduce unstimulated PBL and achieve low-level transgene expression in the absence of any T-cell activation. However, T-cell activation subsequent to the transduction of unstimulated PBL is required for high-level transgene expression. Transduced PBL expressing transgene delivered by the **lentiviral** vectors still preserved resting and naive cell phenotypes. Taken together, prior T cell stimulation and **HIV**-1 accessory proteins are dispensable for **lentivirus**-mediated gene transfer into resting naive and memory T lymphocytes. These results will have significant implications for the study of T-cell biology and for the improvement of clinical gene therapies of acquired immune deficiency syndrome (AIDS) and cancer.

L43 ANSWER 2 OF 3 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:165713 BIOSIS
DOCUMENT NUMBER: PREV200400161037
TITLE: **Lentiviral** transfert of a dominant negative mutant of FADD in CD34+ hematopoietic progenitors from myelodysplastic syndromes normalizes BFU-E growth and inhibits apoptosis of erythroid differentiated cells.
AUTHOR(S): Claessens, Yann-Erick [Reprint Author]; Dubart-Kupperschmitt, Anne [Reprint Author]; Park, Sophie V. [Reprint Author]; Mariot, Virginie [Reprint Author]; Picard, Francoise; Chretien, Stany [Reprint Author]; Dreyfus, Francois [Reprint Author]; Lacombe, Catherine [Reprint Author]; Mayeux, Patrick [Reprint Author]; Fontenay, Michaela [Reprint Author]
CORPORATE SOURCE: Department of Hematology, Cochin Institute, INSERM U567, Paris, France
SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 912a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Mar 2004
Last Updated on STN: 24 Mar 2004

AB Introduction: Ineffective erythropoiesis of myelodysplastic syndromes (MDS) is partly due to excessive apoptosis of differentiated erythroid cells. We have previously demonstrated that both the death domain receptor Fas and its ligand are overexpressed and that blocking their interaction with the Fas:Fc chimera inhibits apoptosis. In this work, we used the **lentiviral** transfert of a dominant negative form of the Fas-associated death domain (FADD) coding sequence to investigate the role of Fas-mediated signaling in normal and MDS erythropoiesis. Materials and methods: ATG-AU1-FADDdn construct was inserted into the **HIV** -derived **lentiviral** vector TRIPDELTAU3 containing a sequence encoding the EGFP, at the BamHI-XhoI cloning sites downstream the EF1alpha promoter. TRIPDELTAU3-EF1alpha/FADDwt and TRIPDELTAU3-EF1alpha/EGFP vectors were used as controls. CD34+ cells isolated from normal (n=5) and

MDS (n=10) marrows were infected for 2 days with vector particles produced by co-transfections of 293T cells by the TRIP vectors and an encapsidation plasmid **lacking all accessory HIV -1 proteins**. Then, cells were maintained in culture conditions allowing the erythroid differentiation. Cell counting, cytological analysis and immunophenotyping were performed every three days. Transduction efficiency and apoptosis were measured by the percentage of EGFP and annexin V positive cells, respectively. Immature erythroid progenitors ie BFU-E were quantified at day 7 of the liquid culture in clonogenic assays. Results: As expected Fas expression was increased in MDS cultures compared to normal onesl. At day 7, mean percentages of EGFP(+) cells were 57.4+-10.9% and 50.8+-16.3% in TRIPDELTAU3-EF1alpha/FADDdn-transduced MDS (MDS FADDdn) and normal cultures, respectively. BFU-Es' number was significantly increased in MDS FADDdn cells compared to MDS EGFP cells (p=0.047) and normalized compared to controls although it was decreased in MDS FADDwt treated cells compared to MDS EGFP cells (p=0.011). At day 14, the mean percentage of apoptotic cells significantly decreased from 36.2+-13.6% in MDS EGFP to 16.5+-6.5% in MDS FADDdn (p=0.0046). The rate of apoptosis was not modified in normal controls. Furthermore, MDS FADDdn cells were resistant to Fas-dependent induction of apoptosis by the Fas agonist CH11. However, the kinetic of erythroid differentiation in MDS FADDdn cultures remained similar to MDS EGFP and normal cultures. Finally, transduction of MDS cells with TRIPDELTAU3-EF1alpha/FADDwt resulted in a dramatic decrease of the percentages of EGFP(+) or Fas(+) cells suggesting that non transduced and Fas(-) cells were positively selected. Conclusion: These data established the crucial role of Fas-dependent signaling in the abnormal apoptosis of MDS erythroid lineage.

L43 ANSWER 3 OF 3 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2000240070 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10775623
TITLE: A Rev-independent **human immunodeficiency virus** type 1 (**HIV**-1)-based vector that exploits a codon-optimized **HIV**-1 gag-pol gene.
AUTHOR: Kotsopoulou E; Kim V N; Kingsman A J; Kingsman S M; Mitrophanous K A
CORPORATE SOURCE: Retrovirus Molecular Biology Group, Department of Biochemistry, University of Oxford, Oxford OX1 3QU, United Kingdom.
SOURCE: Journal of virology, (2000 May) 74 (10) 4839-52. Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000518
Last Updated on STN: 20000518
Entered Medline: 20000511

AB The **human immunodeficiency virus** (**HIV**) genome is AU rich, and this imparts a codon bias that is quite different from the one used by **human** genes. The codon usage is particularly marked for the gag, pol, and env genes. Interestingly, the expression of these genes is dependent on the presence of the Rev/Rev-responsive element (RRE) regulatory system, even in contexts other than the **HIV** genome. The Rev dependency has been explained in part by the presence of RNA instability sequences residing in these coding regions. The requirement for Rev also places a limitation on the development of **HIV**-based vectors, because of the requirement to provide an accessory factor. We have now synthesized a complete codon-optimized **HIV**-1 gag-pol gene. We show that expression levels are high and that expression is Rev independent. This effect is

due to an increase in the amount of gag-pol mRNA. Provision of the RRE in cis did not lower protein or RNA levels or stimulate a Rev response. Furthermore we have used this synthetic gag-pol gene to produce **HIV** vectors that now **lack all** of the **accessory proteins**. These vectors should now be safer than murine leukemia virus-based vectors.

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=> d his

     (FILE 'HOME' ENTERED AT 15:35:40 ON 21 APR 2005)

     FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 15:35:52 ON 21 APR 2005
L1         63641 S (GRAY, ?)/IN,AU
L2          6393 S (MULLIGAN, ?)/IN,AU
L3        558398 S (LEE, ?)/IN,AU
L4        627388 S L1 OR L2 OR L3
L5             5 S L1 AND L2 AND L3
L6             2 DUPLICATE REMOVE L5 (3 DUPLICATES REMOVED)
L7        627388 S L1 OR L2 OR L3
L8            42 S (KOTSOPOULOU, ?)/IN,AU
L9        392484 S (KIM, ?)/IN,AU
L10          744 S (KINGSMAN, ?)/IN,AU
L11          137 S (MITROPHANOUS, ?)/IN,AU
L12            5 S L8 AND L9 AND L10 AND L11
L13            2 DUPLICATE REMOVE L12 (3 DUPLICATES REMOVED)
L14       393256 S L8 OR L9 OR L10 OR L11
L15       108214 S L7 AND L14
L16       646307 S (HUMAN (S) IMMUNODEFICIENCY (S) VIR?) OR HIV OR LENTIVIR? OR
L17         9889 S L16 AND L7
L18         4794 S L16 AND L14
L19          849 S L16 AND L15
L20         1201 S (CODON (S) OPTIMIZ?)
L21          241 S L16 AND L20
L22            5 S L21 AND L7
L23            2 DUPLICATE REMOVE L22 (3 DUPLICATES REMOVED)
L24           14 S L21 AND L14
L25            8 DUPLICATE REMOVE L24 (6 DUPLICATES REMOVED)
L26        65288 S (GAGPOL OR GAG OR POL)
L27          142 S L26 AND L20
L28           20 S L27 AND (L7 OR L14)
L29            2 S L28 NOT (L22 OR L24)
L30            1 DUPLICATE REMOVE L29 (1 DUPLICATE REMOVED)
L31      4339034 S (LACK? OR DEVOID? OR DEFICIENT? OR "WITHOUT")
L32         2584 S ("CTE" OR "CTES" OR (CONSTITUTIVE (S) TRANSPORT (S) ELEMENT))
L33        34022 S ("RRE" OR "REV" OR (REV (S) RESPONSE (S) ELEMENT?))
L34         2598 S ("CTE" OR "CTES" OR (CONSTITUTIVE (S) TRANSPORT (S) ELEMENT?)
L35        36410 S L33 OR L34
L36          870 S L31 (S) L35
L37          428 S L36 AND L16
L38            5 S L37 AND L20
L39            2 DUPLICATE REMOVE L38 (3 DUPLICATES REMOVED)
L40          171 S ALL (S) ACCESSORY (S) (FACTORS OR PROTEINS OR POLYPEPTIDES)
L41           11 S L40 (S) L31
L42            9 S L41 AND L16
L43            3 DUPLICATE REMOVE L42 (6 DUPLICATES REMOVED)
```

Day : Thursday
Date: 4/21/2005

Time: 17:03:21

PALM INTRANET

Inventor Information for 09/393795

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Appln Info | Contents | Petition Info | Atty/Agent Info | Continuity Data | Foreign Data

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PCT / [ ] / [ ] Search **or PG PUBS #** [ ] Search

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